Program Announcement

for the

Defense Health Program

Defense Medical Research and Development Program

Department of Defense

Congressionally Directed Medical Research Programs

Peer Reviewed Medical Research Program

Technology/Therapeutic Development Award

Funding Opportunity Number: W81XWH-14-PRMRP-TTDA

Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Deadline:** 5:00 p.m. Eastern time (ET), June 25, 2014
- **Invitation to Submit an Application:** August 2014
- **Application Submission Deadline:** 11:59 p.m. ET, October 17, 2014
- **End of Application Verification Period:** 5:00 p.m. ET, October 22, 2014
- **Peer Review:** December 2014
- **Programmatic Review:** March 2015

Change for Fiscal Year 2014: *The CDMRP eReceipt System has been replaced with the electronic Biomedical Research Application Portal (eBRAP). Principal Investigators and organizational representatives should register in eBRAP as soon as possible. All pre-applications must be submitted through eBRAP. In addition, applications submitted through Grants.gov will now be available for viewing, modification, and verification in eBRAP prior to the end of the application verification period.*

This Program Announcement/Funding Opportunity is one of two documents with instructions to prepare and submit an application for this funding opportunity. The second document, the General Application Instructions, is available for downloading from Grants.gov.

TABLE OF CONTENTS

I. Funding Opportunity Description 3
A. Program Description 3
B. FY14 PRMRP Topic Areas 3
C. Award Information 4
D. Eligibility Information 7
E. Funding 7
II. Submission Information 9
A. Where to Obtain the Application Package 10
B. Pre-Application Submission and Content Form 10
C. Application Submission Content and Forms 12
D. Verification of Grants.gov Application in eBRAP 18
E. Submission Dates and Times 18
F. Other Submission Requirements 18
III. Application Review Information 19
A. Application Review and Selection Process 19
B. Application Review Process 19
C. Recipient Qualification 22
D. Application Review Dates 22
E. Notification of Application Review Results 22
IV. Administrative Actions 22
A. Rejection 22
B. Modification 22
C. Withdrawal 23
D. Withhold 23
V. Award Administration Information 24
A. Award Notice 24
B. Administrative Requirements 24
C. National Policy Requirements 24
D. Reporting 24
E. Award Transfers 24
VI. Agency Contacts 24
A. CDMRP Help Desk 24
B. Grants.gov Contact Center 25
VII. Application Submission Checklist 26
APPENDIX: Identified Gaps and Research Priorities 27

I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

Applications to the Fiscal Year 2014 (FY14) Peer Reviewed Medical Research Program (PRMRP) are being solicited for the Assistant Secretary of Defense for Health Affairs, Defense Health Program (DHP), by the U.S. Army Medical Research Acquisitions Activity (USAMRAA). The PRMRP was initiated in fiscal year 1999 (FY99) to provide support for military health-related research of exceptional scientific merit. Appropriations for the PRMRP from FY99 through FY13 totaled $644.5 million (M). The FY14 appropriation is $200M. The PRMRP is administered by the U.S. Army Medical Research and Materiel Command (USAMRMC) through the Congressionally Directed Medical Research Programs (CDMRP).

The vision of the FY14 PRMRP is to improve the health and well-being of all military service members, Veterans, and beneficiaries. The PRMRP challenges the scientific and clinical communities to address at least one of the FY14 Topic Areas with original ideas that foster new directions along the entire spectrum of research and clinical care. The program seeks applications in laboratory, clinical, behavioral, epidemiologic, and other areas of research to advance knowledge in disease etiology, improve detection, diagnosis, treatment, and quality of life for those affected by a relevant disease or condition, and to develop and validate clinical care or public health guidelines.

B. FY14 PRMRP Topic Areas

All applications for PRMRP funding must specifically address at least one of the Topic Areas as directed by Congress and must be directly relevant to the health care needs of military service members, Veterans, and/or beneficiaries. If the proposed research does not specifically address at least one of the FY14 PRMRP Topic Areas, the Government reserves the right to administratively withdraw the application. The Government also reserves the right to reassign the application's Topic Area if submitted under an inappropriate Topic Area. The FY14 PRMRP Topic Areas are listed below.

- Acupuncture
- Arthritis (other than post-traumatic osteoarthritis and rheumatoid arthritis)
- Chronic Migraine and Post-Traumatic Headaches
- Congenital Heart Disease
- DNA Vaccine Technology for Post-Exposure Prophylaxis
- Dystonia
- Epilepsy
- Food Allergies
- Fragile X Syndrome
- Hereditary Angioedema
- Illnesses Related to Radiation Exposure (excludes cancer)
- Inflammatory Bowel Disease
- Interstitial Cystitis
- Lupus
- Malaria
- Metabolic Disease
- Neuroprosthetics
- Pancreatitis

- Polycystic Kidney Disease
- Post-Traumatic Osteoarthritis
- Psychotropic Medications
- Respiratory Health (excludes lung cancer and mesothelioma)
- Rheumatoid Arthritis
- Segmental Bone Defects
- Tinnitus

Applications addressing any of the above Topic Areas are of interest to the program. Some of the Topic Areas have gaps and priority research areas that have been identified by the Department of Defense (DoD) and the Department of Veterans Affairs (VA). The list may be found in the Appendix of this document. Applicants are encouraged to read and consider these research areas before preparing their applications. The information provided is not exhaustive, and applicants are not restricted to submitting applications that address the identified gaps. Any aspect of research relevant any FY14 PRMRP Topic Area may be considered for funding.

C. Award Information

The PRMRP Technology/Therapeutic Development Award is a product-driven award intended to provide support for the translation of promising preclinical findings into products for clinical applications, including prevention, detection, diagnosis, patient care, and/or quality of life, in at least one of the Congressionally directed FY14 PRMRP Topic Areas. Products in development should be responsive to the health care needs of military service members, Veterans, and/or beneficiaries.

The product(s) to be developed may be pharmacologic agents (drugs or biologics), devices, and/or clinical guidance for standard of care. The Principal Investigator (PI) must provide a transition plan (including potential funding and resources) showing how the product will progress to the next level of development (e.g., clinical trials, delivery to the military or civilian market) after the completion of the PRMRP award.

Examples of the types of research that may be supported include, but are not limited to:

- Developing and validating clinical guidance/guidelines for standard of care;
- Testing new therapeutic modalities (agents, delivery systems, and chemical modification of lead compounds) using established or validated preclinical systems (PIs seeking funding for establishing or validating preclinical systems should apply to the FY14 PRMRP Investigator-Initiated Research Award mechanism, W81XWH-14-PRMRP-IIRA);
- Designing and implementing pilot or full-scale Good Manufacturing Practice (GMP) production of therapeutics and/or delivery systems for use in advanced preclinical and initial clinical trials;
- Developing pharmacologic agents through adsorption, distribution, metabolism, excretion, and toxicity (ADMET) studies;
- Developing pharmacologic agents to Investigational New Drug (IND) stage for initiation of Phase I clinical trials;

- Developing prototype devices to Investigational Device Exemption (IDE) stage for initiation of clinical trials; and
- Optimizing diagnostic or treatment devices for field deployment.

Applications must include relevant data that supports the rationale for the proposed study. These data may be unpublished and/or from the published literature.

Research involving human subjects and human anatomical substances is permitted; however, ***this award may not be used to conduct clinical trials***. A clinical trial is defined as a prospective accrual of human subjects where an intervention (e.g., device, drug, biologic, surgical procedure, rehabilitative modality, behavioral intervention, or other) is tested on a human subject for a measurable outcome with respect to exploratory information, safety, effectiveness, and/or efficacy. This outcome represents a direct effect on the human subject of that intervention or interaction. For more information on how to distinguish clinical research from clinical trials, see the Human Subject Resource Document at https://ebrap.org/eBRAP/public/Program PIs seeking funding for a clinical trial should apply to the FY14 PRMRP Clinical Trial Award mechanism (W81XWH-14-PRMRP-CTA).

Military Relevance: Relevance to the health care needs of military service members, Veterans, and beneficiaries is a key feature of this award. Investigators are encouraged to consider the following characteristics as examples of how a project may demonstrate military relevance:

- Explanation of how the project addresses an aspect of the target disease/condition that has direct relevance to military service members, Veterans, or other military health system beneficiaries
- Use of military or Veteran populations or data in the proposed research
- Collaboration with DoD or VA investigators
- Involvement of military consultants (Army, Air Force) or specialty leaders (Navy, Marine Corps) to the Surgeons General in a relevant specialty area

PIs are strongly encouraged to collaborate, integrate, and/or align their research projects with DoD and/or VA research laboratories and programs. While not a complete list, the following websites may be useful in identifying additional information about ongoing DoD and VA areas of research interest or potential opportunities for collaboration within the FY14 PRMRP Topic Areas:

Air Force Research Laboratory
http://www.wpafb.af.mil/afrl

Armed Forces Radiobiology Research Institute http://www.usuhs.edu/afrri/

Clinical and Rehabilitative Medicine Research Program
https://crmrp.amedd.army.mil

Combat Casualty Care Research Program
https://ccc.amedd.army.mil

Congressionally Directed Medical Research Programs
http://cdmrp.army.mil

Defense Advanced Research Projects Agency
http://www.darpa.mil/

Defense Medical Research and Development Program
http://dmrdp.fhpr.osd.mil/home.aspx

Defense Technical Information Center
http://www.dtic.mil

Military Infectious Disease Research Program
https://midrp.amedd.army.mil

Military Operational Medicine Research Program
https://momrp.amedd.army.mil

Naval Health Research Center
http://www.med.navy.mil/sites/nhrc

Navy and Marine Corps Public Health Center
http://www.nmcphc.med.navy.mil/

Office of Naval Research
http://www.med.navy.mil/

Office of the Under Secretary of Defense for Acquisition, Technology and Logistics
http://www.acq.osd.mil/

Uniformed Services University of the Health Sciences
http://www.usuhs.edu/research.html

U.S. Army Medical Research Acquisition Activity
https://www.usamraa.army.mil/

U.S. Army Medical Research and Materiel Command
https://mrmc.amedd.army.mil

U.S. Army Research Laboratory
http://www.arl.army.mil

U.S. Department of Defense Blast Injury Research Program
https://blastinjuryresearch.amedd.army.mil/

U.S. Department of Veterans Affairs, Office of Research and Development
http://www.research.va.gov

U.S. Naval Research Laboratory
http://www.nrl.navy.mil

Walter Reed Army Institute of Research
http://wrair-www.army.mil

Use of Active Duty Military and VA Populations: If the proposed research plan involves access to active duty military and/or VA patient populations or resources, the PI is responsible for establishing such access. If possible, access to target active duty military and/or VA patient populations/resources should be confirmed at the time of application submission by inclusion of a letter of support, signed by the lowest ranking person with approval authority, for studies involving active duty military service members, Veterans, military and/or VA controlled study materials, and military and/or VA databases. If access cannot be confirmed at the time of application submission, the Government reserves the right to withhold or revoke funding until the PI has demonstrated support for and access to the relevant population(s) and/or resources. Note that access to a Veteran population for clinical studies may only be obtained by either collaboration with a VA investigator where the VA investigator has a substantial role in the research, or by advertising to the general public.

Use of Human Anatomical Substances, Human Subjects, or Human Cadavers: All DoD-funded research involving new and ongoing research with human anatomical substances, human subjects, or human cadavers must be reviewed and approved by the U.S. Army Medical Research and Materiel Command (USAMRMC) Office of Research Protections (ORP), Human Research Protection Office (HRPO), in addition to the local Institutional Review Board (IRB) of record. Local IRB approval at the time of submission is ***not*** required. The HRPO is mandated to comply with specific laws and requirements governing all research involving human anatomical substances, human subjects, or human cadavers that is supported by the DoD. These laws and requirements will necessitate information in addition to that supplied to the IRB. Allow a minimum of 2 to 3 months for HRPO regulatory review and approval processes. Refer to the General Application Instructions, Appendix 6, for additional information.

New for FY14: **Guidelines for Animal Research:** All projects should adhere to a core set of standards for rigorous study design and reporting to maximize the reproducibility and translational potential of preclinical research. The standards are described in Landis, S.C., et al. A call for transparent reporting to optimize the predictive value of preclinical research. *Nature* 2012, 490:187-191 (www.nature.com/nature/journal/v490/n7419/full/nature11556.html). While these standards are written for preclinical studies, the basic principles of randomization, blinding, sample-size estimation, and data handling derive from well-established best practices in clinical studies. Projects that include research on animal models are required to submit Attachment 8 Animal Research Plan, as part of the application package to describe how these standards will be addressed. Applicants should consult the ARRIVE (Animal Research: Reporting *In Vivo* Experiments) guidelines to ensure relevant aspects of rigorous animal research are adequately planned for and, ultimately, reported. The ARRIVE guidelines can be found at http://www.nc3rs.org.uk/page.asp?id=1357.

The Congressionally Directed Medical Research Programs (CDMRP) intends that data and research resources generated under awards funded by this Program Announcement/Funding Opportunity be made available to the research community (which includes both scientific and consumer advocacy communities) and to the public at large. For additional guidance, refer to the General Application Instructions, Appendix 4, Section L.

D. Eligibility Information

- PIs at or above the level of Assistant Professor (or equivalent) are eligible to submit applications.
- Cost sharing/matching is not an eligibility requirement.
- Eligible investigators must apply through an organization. Organizations eligible to apply include national, international, for-profit, non-profit, public, and private organizations.
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

E. Funding

- The maximum period of performance is **3** years.
- The maximum allowable direct costs for the entire period of performance are **$1.5M** plus indirect costs.
- All direct and indirect costs of any subaward (subgrant or subcontract) must be included in the total direct costs of the primary award.
- The applicant may request the entire maximum funding amount for a project that may have a period of performance less than the maximum **3** years.
- Regardless of the period of performance proposed, the applicant may not exceed the maximum allowable direct costs. Indirect costs shall be proposed in accordance with the organization's negotiated rate agreement.

Refer to the General Application Instructions, Section II.C.4., for budget regulations and instructions for the Research & Related Budget. ***For all federal agencies or organizations collaborating with federal agencies, budget restrictions apply as are noted in Section II.C.4. of the General Application Instructions***.

For this award mechanism, direct costs:

Must be requested for:

- Travel costs of up to $1,800 for the PI(s) to disseminate project results at one DoD-sponsored meeting to be specified by the CDMRP during the award performance period. These travel costs are in addition to those allowed for annual scientific/ technical meetings.

May be requested for (not all-inclusive):

- Salary
- Research supplies
- Equipment
- Clinical research costs (clinical trials are not allowed)
- Support for multidisciplinary collaborations
- Travel between collaborating organizations
- Travel costs of up to $1,800 per year to attend scientific/technical meetings in addition to the required meeting described above

Intramural (DoD), other federal agency, and extramural investigators are encouraged to apply to this Program Announcement/Funding Opportunity. An intramural investigator is defined as a DoD military or civilian employee working within a DoD laboratory or medical treatment facility, or working in a DoD activity embedded within a civilian medical center. Intramural applicants and collaborators are reminded to coordinate receipt and commitment of funds through their respective resource managers. It is permissible for an intramural investigator to be named as a collaborator on an application submitted by an extramural investigator. In such cases, the extramural investigator must include a letter from the intramural collaborator's Commander or Commanding Officer that authorizes the involvement of the intramural collaborator.

As required of all applicants to this Program Announcement/Funding Opportunity, if PIs from federal agencies submit applications, they must submit through Grants.gov. Therefore, federal applicants must be familiar with Grants.gov requirements, including the need for an active System for Award Management (SAM) registration and a Data Universal Numbering System (DUNS) number. Refer to Appendix 3 of the General Application Instructions for further information regarding Grants.gov requirements.

Awards to extramural organizations will consist solely of assistance agreements (Cooperative Agreements and Grants). Awards to intramural agencies and other federal agencies will be executed through the Military Interdepartmental Purchase Request (MIPR) or Funding

Authorization Document (FAD) process. Direct transfer of funds from the recipient to a federal agency is not allowed except under very limited circumstances. Refer to the General Application Instructions, Section II.C.4. Research & Related Budget, for additional information on budget considerations for applications involving federal agencies.

The CDMRP expects to allot approximately $13.5M of the $200M FY14 PRMRP appropriation to fund approximately six Technology/Therapeutic Development Award applications, depending on the quality and number of applications received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of federal funds for this program.

II. SUBMISSION INFORMATION

Submission is a two-step process requiring both (1) pre-application submission through the electronic Biomedical Research Application Portal (eBRAP) (https://eBRAP.org/) and (2) application submission through Grants.gov (http://www.grants.gov/).

New for FY14: ***The CDMRP has replaced its eReceipt System with eBRAP.*** Submission remains a two-step process requiring both pre-application and application submission.

PIs must be registered in eBRAP in order to submit a pre-application and receive notification of the status of a pre-application or application. A key feature of eBRAP is that an organization's representatives and PIs are able to view and modify the Grants.gov application submissions associated with them, but only if the organization, Business Officials, and PIs are registered and affiliated to the organization in eBRAP (see *eBRAP User Guide* at *https://ebrap.org/eBRAP/public/UserGuide.pdf)*. Upon completion of an organization's registration in eBRAP and approval by the CDMRP Help Desk, the organization name will be displayed in eBRAP to assist the organization's business officials and PIs as they register.

Note: Submission of either the pre-application to eBRAP or application to Grants.gov does not require registering an organization and affiliating its Business Officials and PIs in eBRAP; however, the ability to view and modify the Grants.gov application in eBRAP is contingent upon the registration and affiliation. ***Application viewing, modification, and verification in eBRAP is strongly recommended, but not required. The Project Narrative and Budget cannot be changed after the application submission deadline. Any other application component cannot be changed after the end of the application verification period.*** If verification is not completed by the end of the application verification period, the application will be reviewed as submitted through Grants.gov, provided there is no cause for administrative rejection of the application (see Section IV.A., Rejection).

Submission of applications that are essentially identical or propose essentially the same research project to different funding opportunities within the same program and fiscal year is prohibited and will result in administrative withdrawal of the duplicative application.

A. Where to Obtain the Application Package

To obtain the complete application package, including all required forms, perform a Grants.gov (http://www.grants.gov/) basic search using the Funding Opportunity Number: W81XWH-14-PRMRP-TTDA.

B. Pre-Application Submission and Content Form

All pre-application components must be submitted by the PI through eBRAP (https://eBRAP.org/). Because the invitation to submit an application is based on the contents of the pre-application, investigators should not change the title or research objectives after the pre-application is submitted.

PIs and organizations identified in the pre-application should be the same as those intended for the subsequent application submission. If any changes are necessary after submission of the pre-application, the PI must contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507.

The pre-application consists of the following components, which are organized in eBRAP by separate tabs (refer to the General Application Instructions, Section II.B., for additional information on pre-application submission):

- **Application Information – Tab 1**
- **Application Contacts – Tab 2**
    - It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.
- **Collaborators and Conflicts of Interest (COI) – Tab 3**

  FY14 PRMRP Joint Programmatic Review Panel (JPRP) members should not be involved in any pre-application or application. For questions related to JPRP members and pre-applications or applications, refer to Section IV.C., Withdrawal, or contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507.
- **Required Files – Tab 4**

  Notes: Upload document(s) as individual PDF files unless otherwise noted. eBRAP will not allow a file to be uploaded if the number of pages exceeds the limit specified below.

  Preproposal Narrative (two-page limit): The Preproposal Narrative page limit applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings, etc.) used to describe the project. Inclusion of URLs that provide additional information to expand the Preproposal Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the pre-application.

  The Preproposal Narrative should include the following:

    - **Topic Area:** Indicate how the proposed project relates to at least one FY14 PRMRP Topic Area.

- **Technology/Therapeutic Development Product:** Describe the proposed product and briefly compare to existing technologies/therapeutics, as applicable. State the scientific rationale and preclinical findings that support the need for the proposed product.
- **Research Strategy**: State the hypothesis to be tested or the objective(s) to be reached. State the project's specific aims and briefly describe the experimental design and methodology.
- **Personnel:** Briefly state the qualifications of the PI and key personnel to perform the described research project. Note any military- or VA-relevant collaborations.
- **Impact and Military Relevance:** Describe the potential short-term and long-term impact of the results of the proposed study on the research field and the patient population(s) relevant to at least one of the FY14 PRMRP Topic Areas. Explain how the project is relevant to the health care needs of military service members, Veterans, and/or beneficiaries.

Pre-Application Supporting Documentation: The items to be included as supporting documentation for the pre-application ***must be uploaded as individual documents*** and are limited to:

- References Cited (one-page limit): List the references cited (including URLs if available) in the Preproposal Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).
- List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols used in the Preproposal Narrative.
- Key Personnel Biographical Sketch (four-page limit per individual)

- **Submit Pre-Application – Tab 5**

  This tab must be completed for the pre-application to be accepted and processed.

Pre-Application Screening

- **Pre-Application Screening Criteria**

  To determine the technical merits of the pre-application and the relevance to the mission of the DHP and the PRMRP, pre-applications will be screened based on the following criteria:

  - **Technology/Therapeutic Development Product:** How well the pre-application defines a product (e.g., drug, device, clinical guidelines) that will address an unmet need in prevention, detection, diagnosis, patient care, and/or quality of life for a patient population relevant to a FY14 PRMRP Topic Area. How well the proposed research demonstrates sound scientific rationale.
  - **Research Strategy:** How well the specific aims and proposed methodology support the research objectives and the development of the technology or therapeutic.

- **Personnel:** How the personnel's background and expertise are appropriate to accomplish the proposed research.
- **Impact and Military Relevance:** Whether the potential immediate and long-range outcome(s)/product(s) (intellectual and/or tangible) of the proposed research, if successful, will impact a central critical problem or question in the field of research and/or patient care in the FY14 PRMRP Topic Area(s) addressed. How well the research will address a health care issue relevant to military service members, Veterans, and/or beneficiaries

- **Notification of Pre-Application Screening Results**

  Following the pre-application screening, PIs will be notified as to whether or not they are invited to submit applications; however, they will not receive feedback (e.g., a critique of strengths and weaknesses) on their pre-application. The estimated timeframe for notification of invitation to submit an application is indicated on the title page of this Program Announcement/Funding Opportunity.

C. Application Submission Content and Forms

Applications will not be accepted unless the PI has received notification of invitation.

Each application submission must include the completed application package of forms and attachments provided in Grants.gov for this Program Announcement/Funding Opportunity. The application package is submitted by the Authorized Organizational Representative through the Grants.gov portal (http://www.grants.gov/).

New for FY14: ***Applications submitted through and validated by Grants.gov will be retrieved and processed by eBRAP to allow for review, modification, and verification.*** The PI and organizational representatives will receive an email request from eBRAP to review, modify, and verify the application submitted to Grants.gov. During this verification period, the PI may upload missing files (excluding those listed in Section IV.A., Rejection), replace files, and re-categorize files. These modifications must be completed by the end of the verification period.

Note: Changes to either the Project Narrative or Budget are not allowed in eBRAP; if such changes are required, the entire application package must be submitted through Grants.gov as a "Changed/Corrected Application" with the Previous Grants.gov Tracking ID ***prior to the application submission deadline (which occurs earlier than the end of the application verification period).***

Grants.gov application package components: For the Technology/Therapeutic Development Award, the Grants.gov application package includes the following components (refer to the General Application Instructions, Section II.C., for additional information on application submission):

1. **SF 424 (R&R) Application for Federal Assistance Form:** Refer to the General Application Instructions, Section II.C., for detailed information.

2. Attachments Form

- **Attachment 1: Project Narrative (15-page limit):** Upload as "ProjectNarrative.pdf." The page limit of the Project Narrative applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings, etc.) used to describe the project. Inclusion of URLs that provide additional information to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and will result in administrative withdrawal of the application.

  Describe the proposed project in detail using the outline below.

  - **Background:** State the FY14 PRMRP Topic Area(s) addressed by the proposed study. Present the ideas and reasoning behind the proposed work. Cite relevant literature. Describe previous experience most pertinent to the project. Include relevant preliminary data; these data may be unpublished or from the published literature.
  - **Hypothesis or Objective:** State the hypothesis to be tested or the objective to be reached.
  - **Specific Aims:** Concisely explain the project's specific aims. These aims should agree with the primary aims and associated tasks described in the Statement of Work. If the proposed work is part of a larger study, present only aims that the DoD award would fund.
  - **Research Strategy:** Describe the experimental design, methods, and analyses, including appropriate controls, in sufficient detail for analysis. Provide a well-developed, well-integrated research strategy that supports the translational feasibility and promise of the approach. Define the specific study outcomes and how they will be measured. Address potential problem areas and present alternative methods and approaches. Clearly describe the statistical plan and the rationale for the statistical methodology as well as an appropriate power analysis, if applicable. If animal studies are proposed, briefly describe the key elements of the study/studies as they relate to the overall project; detailed information is required in Attachment 8, Animal Research Plan. If human subjects or human biological samples will be used, describe the study population and include a detailed plan for the recruitment of human subjects or the acquisition of samples. Describe the availability of the proposed study population and past successes in recruiting similar populations. ***Clinical trials are not allowed under the Technology/Therapeutic Development Award.***

- **Attachment 2: Supporting Documentation.** Start each document on a new page. Combine and upload as a single file named "Support.pdf." If documents are scanned to pdf, the lowest resolution (100 to 150 dpi) should be used. ***There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested may result in the removal of those items or administrative withdrawal of the application.***

  - References Cited: List the references cited (including URLs if available) in the Project Narrative using a standard reference format that includes the full citation

(i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).

- List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols.
- Facilities, Existing Equipment, and Other Resources: Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate whether or not Government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present Government award under which the facilities or equipment items are now accountable. There is no form for this information.
- Publications and/or Patent Abstracts (five-document limit): Include relevant publication URLs and/or patent abstracts. If publications are not publicly available, then a copy/copies of the published manuscript(s) must be included in Attachment 2. Extra items will not be reviewed.
- Letters of Organizational Support: Provide a letter (or letters, if applicable), signed by the Department Chair or appropriate organization official, confirming the laboratory space, equipment, and other resources available for the project.
- Letters of Collaboration: Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work.
- Letters Confirming Access to Military or VA Patient Populations or Resources (if applicable): If the proposed research plan involves access to active duty military and/or VA patient populations or resources, include a letter of support, signed by the lowest ranking person with approval authority, confirming such access. If access cannot be confirmed at the time of application submission, the Government reserves the right to withhold or revoke funding until the PI has demonstrated support for and access to the relevant population(s) and/or resources.
- Intellectual Property
  - Background and Proprietary Information: All software and data first produced under the award are subject to a federal purpose license in accordance with applicable DoD Grant and Agreement Regulations (DoDGAR) requirements. Provide a list of all background intellectual property to be used in the project or provide a statement that none will be used. If applicable, state and identify the proprietary information that will be provided to the Government and indicate whether the applicant will require a waiver of the federal purpose license.
  - Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations.

- Data and Research Resources Sharing Plan: Describe how data and resources generated during the performance of the project will be shared with the research community. Refer to the General Application Instructions, Appendix 4, Section L for more information about the CDMRP expectations for making data and research resources publicly available.

- **Attachment 3: Technical Abstract (one-page limit):** Upload as "TechAbs.pdf."

  Describe the proposed research project including the following elements:

  Background, rationale, hypothesis or objective, specific aims, study design, long-term and short-term impact to the relevant research field and patient population(s), and the relevance of the project to at least one FY14 PRMRP Topic Area.

  The technical abstract is used by all reviewers; of particular importance, programmatic reviewers typically do not have access to the full application and rely on the technical abstract for appropriate description of the project's key aspects. Therefore, clarity and completeness within the space limits of the technical abstract are highly important.

- **Attachment 4: Lay Abstract (one-page limit):** Upload as "LayAbs.pdf."

  State the FY14 PRMRP Topic Area(s) addressed by the proposed research project. Include a comprehensive overview of the proposed research project that can be readily understood by lay persons with nonscientific backgrounds. Clearly describe the central critical problem or question to be addressed and the ultimate applicability and impact of the research. Do not duplicate the technical abstract.

- **Attachment 5: Statement of Work (SOW) (three-page limit):** Upload as "SOW.pdf." Refer to the General Application Instructions, Section II.C.2., for detailed guidance on creating the SOW.

  The suggested SOW format and examples specific to different types of research projects are available on the eBRAP "Program Announcement and Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). For the Technology/ Therapeutic Development Award mechanism, use the SOW format example titled "SOW (Statement of Work) Generic Format" if human subjects will be recruited, otherwise use the format example titled "SOW for Advanced Tech Development Research." The SOW must be in PDF format prior to attaching.

- **Attachment 6: Impact Statement (one-page limit):** Upload as "Impact.pdf."

  Explain why the proposed research project is important and relevant to understanding the cause or progression of the disease or condition, and/or to developing improvements in detection, diagnosis, patient care, or quality of life in the FY14 PRMRP Topic Area(s) addressed. Describe how the study will address a central critical problem or question in the relevant Topic Area(s).

  Describe the short-term impact: Detail the anticipated outcome(s)/product(s) (intellectual and/or tangible) that will be directly attributed to the results of the proposed research.

Describe the long-term impact: Explain the anticipated long-term gains from this research. Compare to the information known/products currently available, if applicable. Explain the long-range vision for how the research will impact clinical care.

- **Attachment 7: Military Relevance Statement (one-page limit):** Upload as "MilRel.pdf."

  Describe how the proposed study is responsive to the health care needs of military service members, Veterans, and/or beneficiaries. Provide information about the incidence and/or prevalence of the disease or condition to be studied in military service members, Veterans, and/or beneficiaries.

  If active duty military, military families, and/or Veteran population(s) or datasets will be used in the proposed research project, describe the population(s)/dataset(s), the appropriateness of the population(s)/dataset(s) for the proposed study, and the feasibility of accessing the population(s)/dataset(s). If a non-military population will be used for the proposed research project, explain how the population simulates the targeted population (i.e., military service members, Veterans, and/or beneficiaries).

  If applicable, show how the proposed research project aligns with DoD and/or VA areas of research interest.

- **Attachment 8: Animal Research Plan (required if the proposed research involves animals, five-page limit):** Upload as "AnimalPlan.pdf."

  When the proposed study involves animals, the applicant is required to submit a summary describing the animal research that will be conducted. Applicants should not submit a verbatim replica of the protocol(s) to be submitted to the Institutional Animal Care and Use Committee (IACUC) as the Animal Research Plan. The Animal Research Plan should address the following points for each proposed animal study:

  - Briefly describe the research objective(s) of the animal study. Explain how and why the animal species, strain, and model(s) being used can address the scientific objectives and, where appropriate, the study's relevance to human biology.
  - Summarize the procedures to be conducted. Describe how the study will be controlled.
  - Describe the randomization and blinding procedures for the study and any other measures to be taken to minimize the effects of subjective bias during animal treatment and assessment of results. If randomization and/or blinding will not be utilized, provide justification.
  - Provide a sample size estimate for each study arm and the method by which it was derived, including power analysis calculations.
  - Describe how data will be handled, including rules for stopping data collection, criteria for inclusion and exclusion of data, how outliers will be defined and

handled, statistical methods for data analysis, and identification of the primary endpoint(s).

- **Attachment 9: Transition Plan (one-page limit):** Upload as "Transition.pdf."

  Provide information on the methods and strategies proposed to move the product or knowledge outcomes to the next phase of development (e.g., clinical trials, commercialization, and/or delivery to the civilian or military market) after successful completion of the award. Applicants are encouraged to work with their organization's Technology Transfer Office to develop the transition plan. The transition plan should include the components listed below.

  - The planned indication for the product label, if appropriate, and an outline of the development plan required to support that indication.
  - Details of the funding strategy that will be used to bring the outcomes to the next level of development and/or commercialization (e.g., specific potential industry partners, specific funding opportunities to be applied for).
  - For knowledge products, a description of how the knowledge will be further developed, disseminated, and incorporated into clinical care.
  - A description of collaborations and other resources that will be used to provide continuity of development.
  - A brief schedule and milestones for bringing the outcome(s) to the next phase of clinical trials, commercialization, and/or delivery to the military or civilian market, including when it can be anticipated to be transitioned to an industry partner or approved by the FDA, if applicable.
  - A risk analysis for cost, schedule, manufacturability, and sustainability.
  - A description of relevant product patents and intellectual property ownership, and their potential impact on product development.

3. **Research & Related Senior/Key Person Profile (Expanded):** Refer to the General Application Instructions, Section II.C.3., for detailed information.

   - PI Biographical Sketch (four-page limit): Upload as "Biosketch_LastName.pdf."
   - PI Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."
   - Key Personnel Biographical Sketches (four-page limit each): Upload as "Biosketch_LastName.pdf."
   - Key Personnel Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

4. **Research & Related Budget:** Refer to the General Application Instructions, Section II.C.4., for detailed information.

   - Budget Justification (no page limit): Upload as "BudgetJustification.pdf."

5. **Project/Performance Site Location(s) Form:** Refer to the General Application Instructions, Section II.C.5., for detailed information.

6. **R & R Subaward Budget Attachment(s) Form (if applicable):** Refer to the General Application Instructions, Section II.C.6., for detailed information.

D. Verification of Grants.gov Application in eBRAP

For FY14, a new process has been initiated whereby organizational representatives and PIs can view their applications as submitted through Grants.gov and prior to peer review of the application. This will enable applicants to make modifications prior to scientific and programmatic evaluation of applications, provided the modifications are made by either the end of the application verification period or, for changes to the Project Narrative or Budget, by the application submission deadline.

After application submission to Grants.gov, eBRAP will retrieve and validate the application submission. eBRAP will notify the organizational representatives and PI via email and instruct them to log into eBRAP to review, modify, and verify the application. Files that fail eBRAP validation will be noted in both the email and in the Full Application Files tab. eBRAP does not validate the accuracy or completeness of content in the files. PIs are strongly encouraged to review all application components. If either the Project Narrative or the Budget fail eBRAP validation, an updated Grants.gov application package must be submitted via Grants.gov prior to the application submission deadline, which occurs earlier than the end of the application verification period. ***The Project Narrative and Budget cannot be changed after the application submission deadline. Any other application component cannot be changed after the end of the application verification period.***

E. Submission Dates and Times

All submission dates and times are indicated on the title page of this Program Announcement/ Funding Opportunity. Pre-application and application submissions are required. Failure to meet either of these deadlines will result in application rejection.

F. Other Submission Requirements

Refer to the General Application Instructions, Appendix 2, for detailed formatting guidelines.

All applications must be submitted through Grants.gov. Applicant organizations and all subrecipient organizations must have a DUNS number to submit applications to Grants.gov. The applicant organization must also be registered in the Entity Management functional area of the SAM with an "Active" status to submit applications through the Grants.gov portal. Refer to the General Application Instructions, Appendix 3, for information on Grants.gov requirements.

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

All applicants are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is peer review of applications against established criteria for determining technical merit. The second tier is a programmatic review that makes recommendations for funding to the Office of the Assistant Secretary of Defense for Health Affairs, based on (a) technical merit and (b) the relevance to the mission of the DHP and PRMRP and to the specific intent of the award mechanism. The highest-scoring applications from the first tier of review are not automatically recommended for funding. Additional information about the two-tier process used by the CDMRP can be found at http://cdmrp.army.mil/about/fundingprocess.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Panel members sign a non-disclosure statement that application and evaluation information will not be disclosed outside the panel. Violations of confidentiality can result in the dissolving of a panel(s) and other corrective actions. In addition, personnel at the applicant or collaborating organizations are prohibited from contacting persons involved in the review process to gain protected evaluation information or to influence the evaluation process. Violations of these prohibitions will result in the administrative withdrawal of the organization's application. Violations by panel members or applicants that compromise the confidentiality of the review process may also result in suspension or debarment from federal awards. Furthermore, the unauthorized disclosure of confidential information of one party to another third party is a crime in accordance with Title 18 United States Code 1905.

B. Application Review Process

1. **Peer Review:** To determine technical merit, all applications will be evaluated according to the following scored criteria, which are listed in decreasing order of importance:

    - **Research Strategy and Feasibility**
        - How well the scientific rationale supports the project and its feasibility, as demonstrated by a critical review and analysis of the literature, supporting data, and logical reasoning.
        - How well the hypotheses or objectives and aims are developed.
        - How well the experimental design, methods, data collection procedures, and analyses are developed and support completion of the aims.
        - The degree to which the expected outcome(s) that will result after completion of the proposed research project are specific and measurable.
        - If applicable, to what degree the statistical plan and power analysis are appropriate for the proposed project.
        - How well the application acknowledges potential problems and addresses alternative approaches.

- If applicable, the degree to which the plan to study patient populations is appropriate and feasible and whether the application provides evidence of availability of and access to the necessary study populations and/or resources.
- Whether the research can be completed within the proposed period of performance.

For applications involving animal research:

- How well the animal study (or studies) is designed to achieve the objectives, including the choice of model and endpoints/outcome measures to be used.
- How well the study (or studies) is designed to achieve reproducible and rigorous results, including controls, sample size estimation, blinding, randomization, and data handling.

- **Impact**
  - For the FY14 PRMRP Topic Area (s) addressed, how the proposed research project, if successful, will:
    - Make important scientific advances in the relevant field of research,
    - Promote greater understanding of the causes and progression of the relevant disease(s)/condition(s),
    - Promote the development of improvements in patient care, and/or
    - Promote the development of improvements in quality of life.
  - How well the project addresses a critical problem in research or patient care for a FY14 PRMRP Topic Area.
  - To what degree the proposed project could, if successful, make a significant impact on the lives of relevant patient populations in the short term or long term.
- **Transition Plan**
  - Whether the funding strategy described to bring the outcome(s) to the next level of development (e.g., clinical trial, transition to industry, delivery to the market, progression toward incorporation into standard practice) is appropriate.
  - How the development plan to support a product label change, if applicable, is appropriate and well described.
  - Whether appropriate collaborations and other resources for providing continuity of development are established and/or well described.
  - How the schedule and milestones for bringing the outcome(s) to the next level of development (e.g., clinical trial, transition to industry, delivery to the market, progression toward incorporation into standard practice) are appropriate.
  - How well the potential risk analysis for cost, schedule, manufacturability, and sustainability is developed.

- How well the application identifies intellectual property ownership, describes any appropriate intellectual and material property plan among participating organizations (if applicable), and addresses any impact of intellectual property issues on product development and subsequent Government access to products supported by this Program Announcement/Funding Opportunity.

- **Personnel**
  - How the background and expertise of the PI(s) and other key personnel demonstrate their ability to perform the proposed work.
  - How the levels of effort by the PI(s) and other key personnel are appropriate to ensure the successful conduct of the project.
  - How the PI(s)'s record(s) of accomplishment demonstrates his/her ability to accomplish the proposed work.

In addition, the following unscored criteria will also contribute to the overall evaluation of the application:

- **Environment**
  - How the scientific environment is appropriate for the proposed research.
  - How the research requirements are supported by the availability of and accessibility to facilities and resources (including collaborative arrangements).
  - How the quality and extent of organizational support are appropriate for the proposed research.
- **Budget**
  - Whether the budget is appropriate for the proposed research and within the limitations of this Program Announcement/Funding Opportunity.
- **Application Presentation**
  - To what extent the writing, clarity, and presentation of the application components influence the review.

2. **Programmatic Review:** To make funding recommendations, the following criteria are used by programmatic reviewers:

   a. **Ratings and evaluations of the peer reviewers**

   b. **Relevance to the mission of the DHP and the FY14 PRMRP, as evidenced by the following:**
      - Adherence to the intent of the award mechanism
      - Military relevance
      - Program portfolio composition
      - Relative impact
      - Relevance to program objectives

C. Recipient Qualification

For general information on required qualifications for award recipients, refer to the General Application Instructions, Appendix 1.

D. Application Review Dates

All application review dates and times are indicated on the title page of this Program Announcement/Funding Opportunity.

E. Notification of Application Review Results

Each PI and organization will receive email notification of posting of the funding recommendation in eBRAP. Each PI will receive a peer review summary statement on the strengths and weaknesses of the application.

IV. ADMINISTRATIVE ACTIONS

After receipt of pre-applications from eBRAP or applications from Grants.gov, the following administrative actions may occur:

A. Rejection

The following will result in administrative rejection of the pre-application:

- Preproposal Narrative exceeds page limit.
- Preproposal Narrative is missing.

The following will result in administrative rejection of the application:

- Submission of an application for which a letter of invitation was not received.
- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Submission of the same research project to different funding opportunities within the same program and fiscal year.

B. Modification

- Pages exceeding the specific limits will be removed prior to review for all documents other than the Preproposal Narrative and Project Narrative.
- Documents not requested will be removed.
- Following application submission to Grants.gov, the PI will receive an email request from eBRAP to review, modify, and verify the application submitted to Grants.gov. During this verification period, the PI may upload missing documents (excluding those listed in Section IV.A., Rejection), replace files, and re-categorize files. These

modifications must be completed by the end of the application verification period; otherwise, the application will be reviewed as submitted.

C. Withdrawal

The following may result in administrative withdrawal of the pre-application or application:

- A FY14 PRMRP JPRP member is named as being involved in the research proposed or is found to have assisted in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting documentation. A list of the FY14 PRMRP JPRP members can be found at http://cdmrp.army.mil/prmrp/panels/panel14.
- The application fails to conform to this Program Announcement/Funding Opportunity description to the extent that appropriate review cannot be conducted.
- Direct costs as shown on the Research & Related Budget exceed the maximum allowed by this Program Announcement/Funding Opportunity.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- Inclusion of any employee of CDMRP review contractors in applications for funding without adequate plans to mitigate conflicts of interest. Refer to the General Application Instructions, Section II.B., for detailed information.
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review process to gain protected evaluation information or to influence the evaluation process.
- The proposed research is, or requests funding for, a clinical trial.
- The PI does not meet the eligibility criteria.
- The proposed research project is not relevant to any of the Congressionally directed FY14 PRMRP Topic Areas.

D. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending institutional investigation. The institution will be required to provide the findings of the investigation to the USAMRAA Grants Officer for a determination of the final disposition of the application.

V. AWARD ADMINISTRATION INFORMATION

A. Award Notice

Awards will be made no later than September 30, 2015. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

B. Administrative Requirements

Refer to the General Application Instructions, Appendix 4 for general information regarding administrative requirements.

C. National Policy Requirements

Refer to the General Application Instructions, Appendix 5 for general information regarding national policy requirements.

D. Reporting

Refer to the General Application Instructions, Appendix 4, Section J, for general information on reporting requirements.

Quarterly technical progress reports and quad charts may be required.

E. Award Transfers

Refer to the General Application Instructions, Appendix 4, Section M, for general information on organization or PI changes.

VI. AGENCY CONTACTS

A. CDMRP Help Desk

Questions related to Program Announcement/Funding Opportunity content or submission requirements as well as questions related to the submission of the pre-application through eBRAP should be directed to the CDMRP Help Desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. ET. Response times may vary depending upon the volume of inquiries.

Phone: 301-682-5507

Email: help@eBRAP.org

B. Grants.gov Contact Center

Questions related to application submission through Grants.gov portal should be directed to the Grants.gov Contact Center, which is available 24 hours a day, 7 days a week (closed on U.S. federal holidays). Note that the CDMRP Help Desk is unable to provide technical assistance with Grants.gov submission.

Phone: 800-518-4726

Email: support@grants.gov

Sign up on Grants.gov for "send me change notification emails" by following the link on the Synopsis page for the Program Announcement/Funding Opportunity or by responding to the prompt provided by Grants.gov when first downloading the application package. If the application package is updated or changed, the original version of the application package may not be accepted by Grants.gov.

VII. APPLICATION SUBMISSION CHECKLIST

Grants.gov Application Components	Action	Completed
SF-424 (R&R) Application for Federal Assistance	Complete form as instructed.	
Attachments Form	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf.".	
	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	Impact Statement: Upload as Attachment 6 with file name "Impact.pdf."	
	Military Relevance Statement: Upload as Attachment 7 with file name "MilRel.pdf."	
	Animal Research Plan: Upload as Attachment 8 with file name "AnimalPlan.pdf," if applicable.	
	Transition Plan: Upload as Attachment 9 with file name Transition.pdf."	
Research & Related Senior/Key Person Profile (Expanded)	Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.	
	Attach PI Previous/Current/Pending Support (Support_LastName.pdf) to the appropriate field.	
	Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person to the appropriate field.	
	Attach Previous/Current/Pending (Support_LastName.pdf) for each senior/key person to the appropriate field.	
Research & Related Budget	Complete form as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field.	
Project/Performance Site Location(s) Form	Complete form as instructed.	
R & R Subaward Budget Attachment(s) Form	Complete form as instructed.	

APPENDIX

IDENTIFIED GAPS AND RESEARCH PRIORITIES

Applications addressing any of the FY14 PRMRP Topic Areas are of interest to the program. Some of the Topic Areas have gaps and priority research areas that have been identified by the DoD and the VA and are listed below. Applicants are encouraged to read and consider these research areas before preparing their applications. The information provided is not exhaustive, and applicants are not restricted to submitting applications that address the identified gaps. Any aspect of research relevant any FY14 PRMRP Topic Area may be considered for funding.

Acupuncture:

- Definitive studies to determine the effectiveness of acupuncture for pain associated with traumatic neuromusculoskeletal injuries.
- Research on the role of acupuncture in pain management following traumatic brain injury, spinal cord injury, and/or peripheral nerve injury.
- Research on the use of acupuncture as prevention of or treatment for mental health disorders such as post-traumatic stress, depression, suicide, substance abuse, agitation, anxiety, and other co-morbid disorders.

Chronic Migraine and Post-Traumatic Headache:

- Epidemiological/natural history studies of post trauma headache to determine specific types of headache encountered, the pathobiology behind these headaches (such as the role of cortical spreading depression acutely after injury as a risk factor for chronic headaches of a migrainous type) as well as risk factors that might predispose people to certain types of post-traumatic headache.
- Double-blind placebo-controlled trials in the post-traumatic headache population in order to determine whether similar phenotypes in primary headache disorders and post-traumatic headache will respond similarly to treatment.
- Research on the optimal approaches to acute and chronic pain management for chronic migraine and post-traumatic headache, with a focus on assessing and eliminating adverse outcomes.
- Research on the utility of the Patient Centered Medical Home model in care of patients with chronic migraine or post-traumatic headache.
- Research to investigate, develop, and validate biomarkers useful in diagnosing and monitoring traumatic brain injury patients with chronic migraine or post-traumatic headache.

DNA Vaccine Technology for Post-Exposure Prophylaxis:

- The design and manufacture of a cost-efficient DNA vaccine that is simple to manufacture, stable without the need for refrigeration or freezing, can be used in both immune-competent and immune-compromised individuals, and expresses a highly conserved, chimeric protein antigen displaying multiple antigenic domains of key virulence factors of enteric pathogens.

- Development of innovative approaches to cure HIV (human immunodeficiency virus) using multiple therapeutic modalities in acute HIV infection. Additionally, there is a need to optimize antibody responses using novel adjuvants for HIV vaccine.
- Development of mechanisms or devices for mucosal delivery of a DNA vaccine for enteric pathogens. This includes research to understand and improve the mechanisms to stimulate immune responses with a cost-efficient DNA vaccine for enteric pathogens that is simple to manufacture and stable without the need for refrigeration or freezing.
- Research leading to a better understanding of the immune mechanisms involved in the clearance of enteric pathogens that would most likely be stimulated by a DNA vaccine. There is a need to evaluate humoral immune responses after DNA vaccination and to determine immunological correlates of protection, including both antibodies and cellular immune mechanisms in reproducible small animal models.

Epilepsy:

- Epidemiological and pathobiological studies that will inform early diagnosis, monitoring, and evidence-based treatment guidelines for seizure disorders.
- Pharmacologic and non-pharmacologic interventions demonstrating objective improvement in measureable outcomes of decreased seizure frequency.
- Development of technologies that can identify prodromal markers of epileptiform activity so that the patient can medicate and/or find a safe place to rest before the seizure occurs.

Illnesses Related to Radiation Exposure:

- Research addressing acute radiation syndrome (ARS).
- Research addressing the delayed effects of acute radiation exposure (DEARE).
- Research related to qualification of drug development tools (biomarkers, clinical outcome assessments, or animal models).
- Research on prototype countermeasures with the intent to develop data to support FDA approval.

Inflammatory Bowel Disease:

- Studies on the long-term health consequences of acute enteric infection as they relate to inflammatory bowel disease (IBD) in the areas of epidemiology, animal model development, understanding disease pathogenesis, and development of effective preventive and clinical management modalities.
- Studies designed specifically to examine disease markers (genetic, microbiomic, immunologic) of severity or risk of IBD after acute enteric infections.
- Mechanistic studies in relevant post-infectious inflammatory disease animal models to elucidate the interactions among genomics, microbiome, and immune mechanisms behind infection and chronic health consequences.
- Studies of well-defined post-infectious IBD patients are needed to provide estimates of illness-associated disability, health care costs, and symptom duration from a military health system and societal perspective.

Malaria:

- Development and optimization of multi-platform based (i.e., protein, DNA, viral vector or live-attenuated) pre-erythrocytic based malaria vaccines to increase efficacy and enable identification of correlates of protection in preclinical studies and clinical trials.
- Identification of novel pre-erythrocytic stage *Plasmodium vivax* antigens and assessment of potential predictors of candidate vaccine efficacy in preclinical studies and clinical trials.
- Development of orally administered, bioavailable, novel chemical entities or alternative formulations of known anti-malarial drugs suitable for weekly prophylaxis, radical cure, treatment of severe/complicated disease indications, and to replace artemisinin class drugs in targeting immature blood stage parasites.
- Identification of modes of action of new generation anti-malarial drugs, optimization of drug partnering strategies for new malaria therapeutics and prophylaxis indications, and characterization of interactions between 8-aminoquinoline class anti-malarial drugs and cytochrome p450 2D6 enzyme to optimize development of next-generation anti-malarial drugs.

Neuroprosthetics:

- Advancement of efferent control, i.e., control of multi degree-of-freedom prostheses. This could include an upper extremity with fine motor movements, or a lower extremity to provide a biologically accurate gait.
- Development of device afferent communication, science of proprioception and pressure sensing and how to communicate this information to the user. The end goal of this research would be for the user to obtain natural feedback from a terminal device.

Post-Traumatic Osteoarthritis:

- Development of best practices to maximize function and evaluation of multidisciplinary team (orthopaedics, pain, rehabilitation, etc.) approaches evaluating the success of treatment algorithms.
- Technologies that restore joint stability after injury (e.g., connective tissues such as ligament/ tendon/meniscus structures).
- Sustained release, intra-articular injectable steroidal, non-steroidal, or disease-modifying therapies that offer two or more months of symptomatic relief of pain and/or inflammation in a single injection.
- Development of preventive therapies and/or techniques to minimize the progression of post-traumatic osteoarthritis after traumatic injury to the joint.

Psychotropic Medications:

- Identification and/or development of therapies that can completely or selectively reverse the effects of psychotropic medications.
- Research into the use of psychotropic medications for the treatment of mental health disorders including post-traumatic stress, suicide, substance abuse, and other co-morbid disorders.

- Research to determine and test psychological interventions related to mental health issues specific to women in the military.

Respiratory Health:

- Development of an innovative, next-generation Adenovirus vaccine, ideally one that may be modified for different adenovirus serotypes, for the prevention of acute respiratory illness caused by Adenovirus.
- Research into opportunistic infections that will assist in understanding their basic metabolism, create ex vivo growth systems or small animal models where there are none available, and/or develop new agents with which to treat them as it relates to respiratory disease.
- Technology- and/or therapeutic-based treatments for acute lung injury due to an inhalational injury
- Preventive techniques and therapeutics to reduce the incidence of acute respiratory syndrome after acute lung injury in trauma patients.
- Research on the prevalence, cause, treatment, and prevention of respiratory symptoms and ailments possibly associated with deployed and re-deployed military personnel, including acute eosinophilic pneumonia, constrictive bronchiolitis, asthma, allergies, and other chronic lung diseases and breathing problems.

Segmental Bone Defects:

- Technologies addressing segmental/large bone defects in the craniomaxillofacial body region.
- Controlled release/extended release of growth factors for bone regeneration.
- Technologies that enable enhanced recruitment of endogenous cell populations for bone regeneration.
- Technologies that repair the soft tissue envelope to enhance bone regeneration.

Tinnitus:

- Research to understand the mechanisms of tinnitus, its relationship to noise-induced hearing loss, and progression to chronic tinnitus.
- Identification of effective non-invasive interventions to include neuromodulation and tinnitus retraining therapy for tinnitus treatment.
- Identification of novel therapies for early interventions to prevent tinnitus, including new uses for existing drugs, nutritional and pharmaceutical based strategies, and acoustic, electrical, and other stimulation technologies.
- Improvement of objective tools to diagnose and characterize tinnitus (e.g., imaging techniques to identify functional and structural changes in the brain).